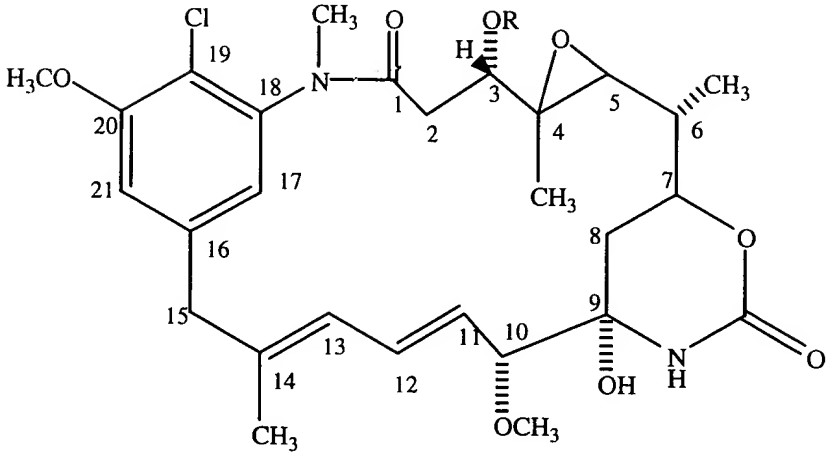
FIG. 1



1a $COCH(CH_3)N(CH_3)COCH_3$

1b H

FIG. 2

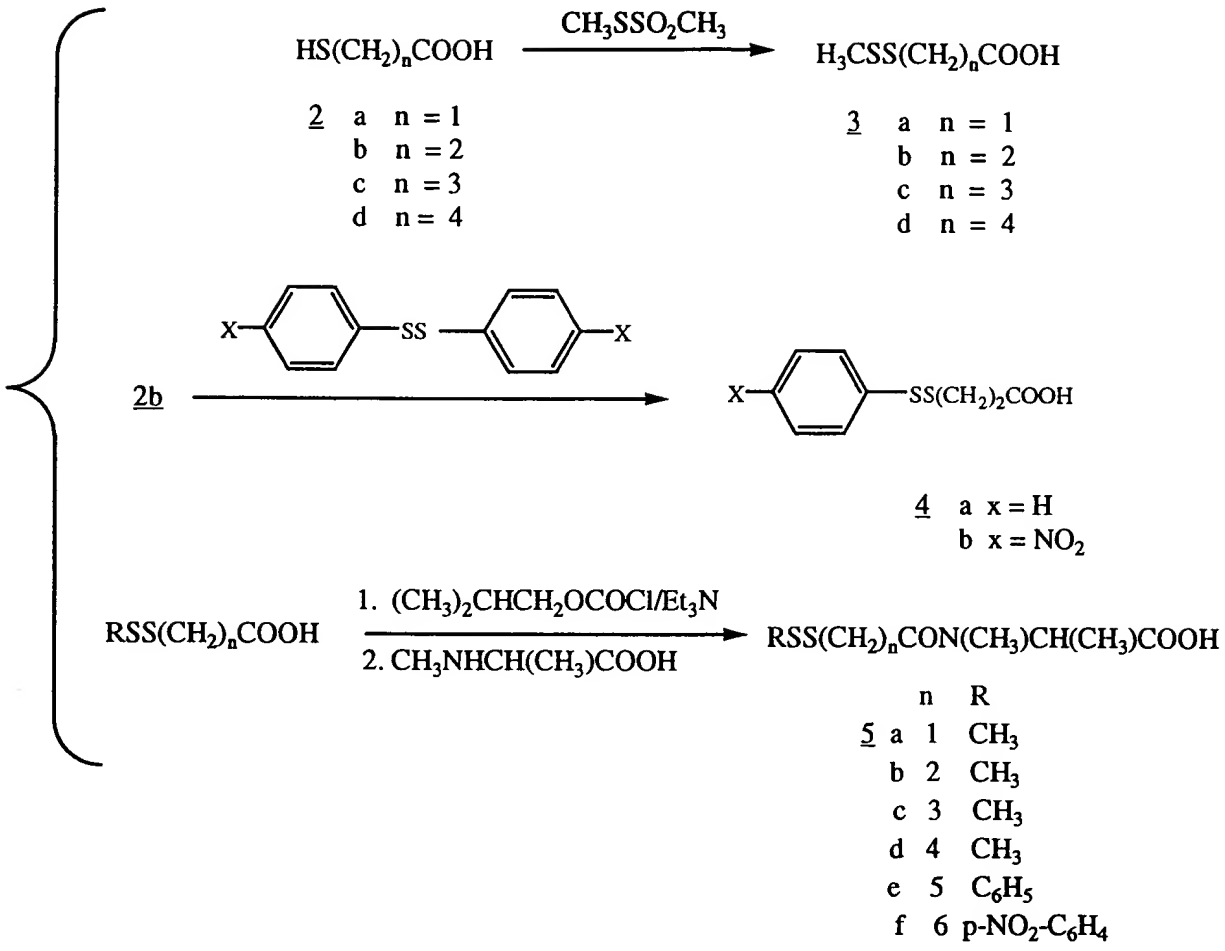

HS(CH2)nCOOH
CH3SSO2CH3
H3CSS(CH2)nCOOH
2 a n = 1
b n = 2
c n = 3
d n = 4
3 a n = 1
b n = 2
c n = 3
d n = 4
X
SS
X
2b
X
SS(CH2)2COOH
4 a x = H
b x = NO2
RSS(CH2)nCOOH
1. (CH3)2CHCH2OCOCl/Et3N
2. CH3NHCH(CH3)COOH
RSS(CH2)nCON(CH3)CH(CH3)COOH
n R
5 a 1 CH3
b 2 CH3
c 3 CH3
d 4 CH3
e 5 C6H5
f 6 p-NO2-C6H4

FIG. 3

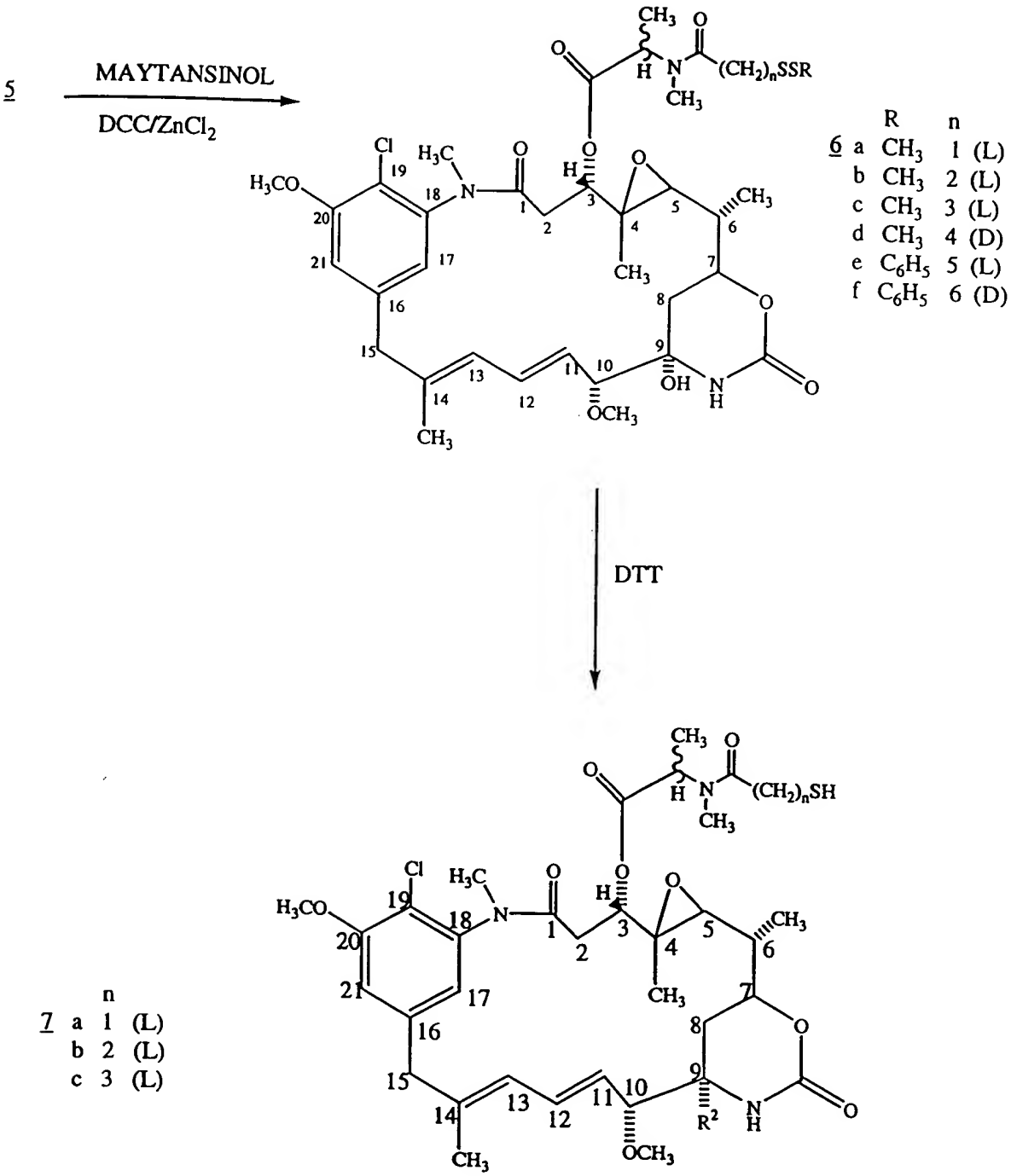

5
MAYTANSINOL
DCC/ZnCl2
6 a CH3 1 (L)
b CH3 2 (L)
c CH3 3 (L)
d CH3 4 (D)
e C6H5 5 (L)
f C6H5 6 (D)
DTT
7 a 1 (L)
b 2 (L)
c 3 (L)

FIG. 4a

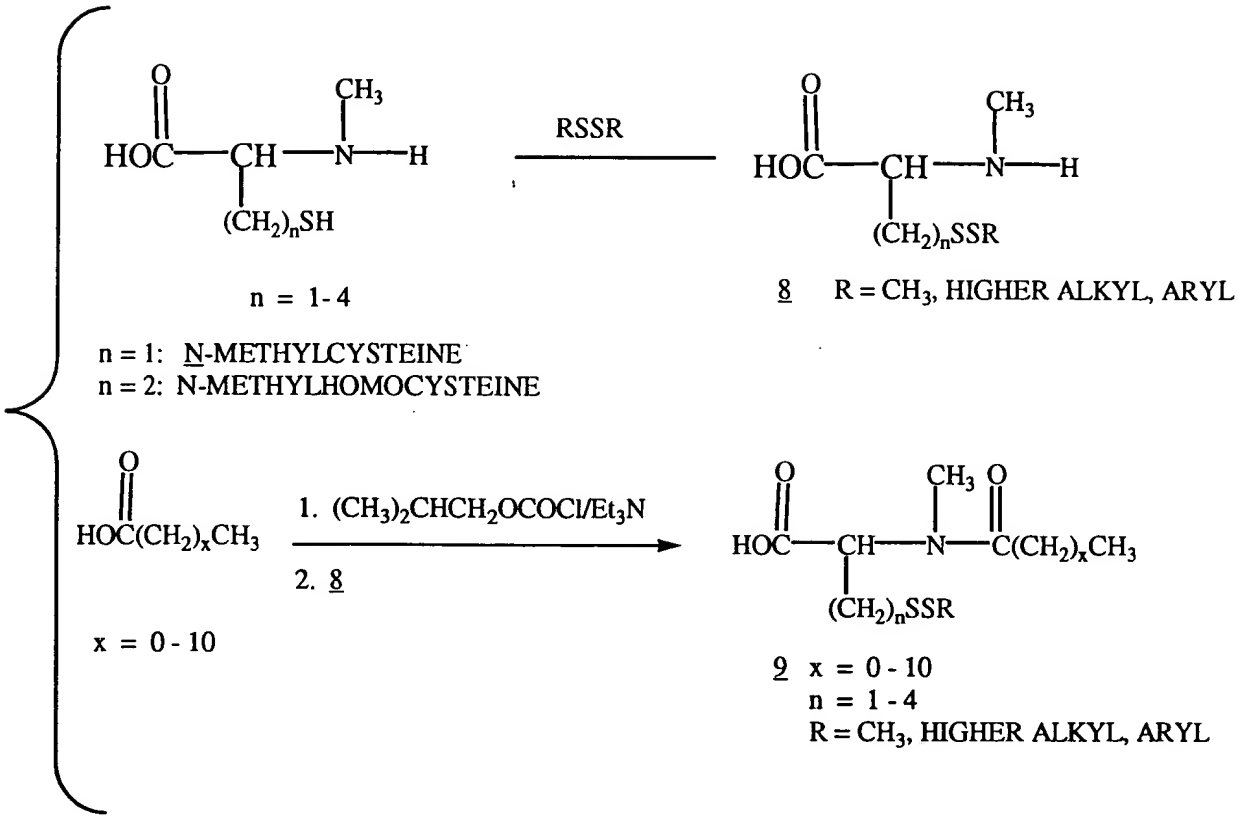

HOC—CH(CH3)—N(CH3)—H
(CH2)nSH
RSSR
HOC—CH(CH3)—N(CH3)—H
(CH2)nSSR
n = 1-4
8 R = CH3, HIGHER ALKYL, ARYL
n = 1: N-METHYLCYSTEINE
n = 2: N-METHYLHOMOCYSTEINE
HOC(CH2)xCH3
1. (CH3)2CHCH2OCOCl/Et3N
2. 8
HOC—CH(CH3)—N(CH3)—C(CH2)xCH3
(CH2)nSSR
x = 0 - 10
9 x = 0 - 10
n = 1 - 4
R = CH3, HIGHER ALKYL, ARYL

FIG. 4b

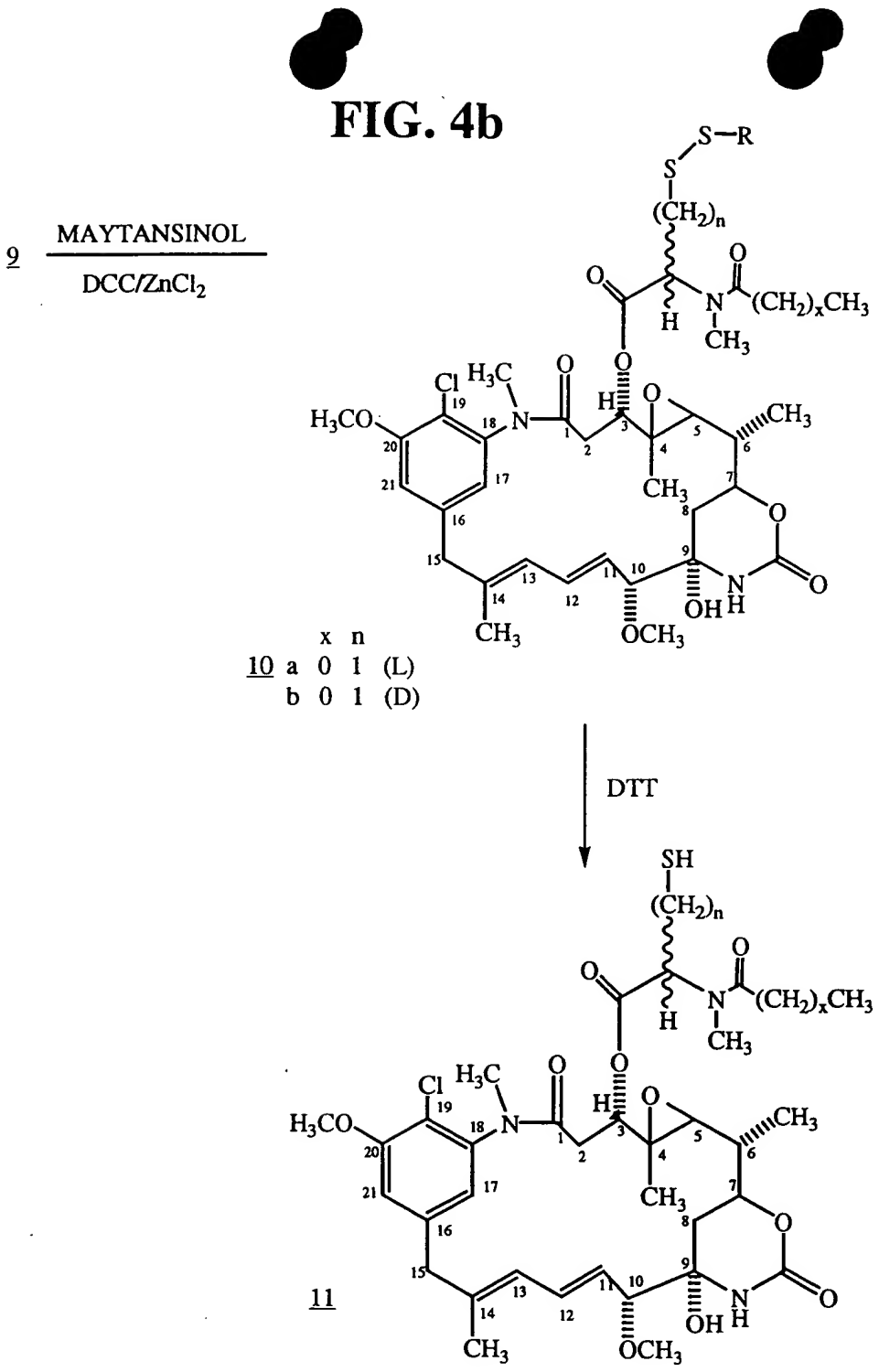

9
MAYTANSINOL
DCC/ZnCl2
S—R
S
(CH2)n
O
N
(CH2)xCH3
H
CH3
H3C
Cl
H3CO
CH3
OH
OCH3
x n
10 a 0 1 (L)
b 0 1 (D)
DTT
SH
11

FIG. 5

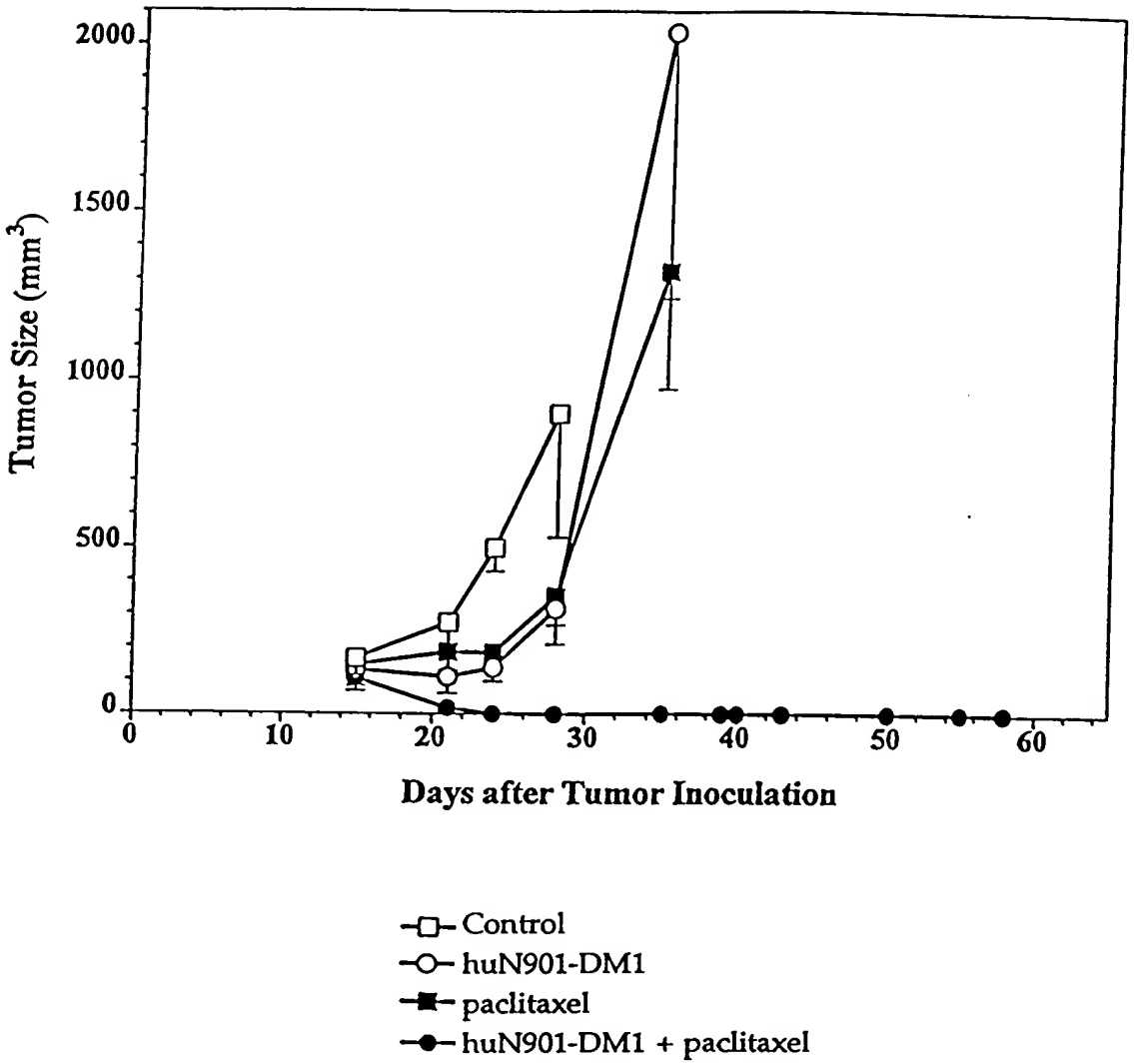

2000
1500
1000
500
0
Tumor Size (mm3)
0
10
20
30
40
50
60
Days after Tumor Inoculation
Control
huN901-DM1
paclitaxel
huN901-DM1 + paclitaxel

FIG. 6

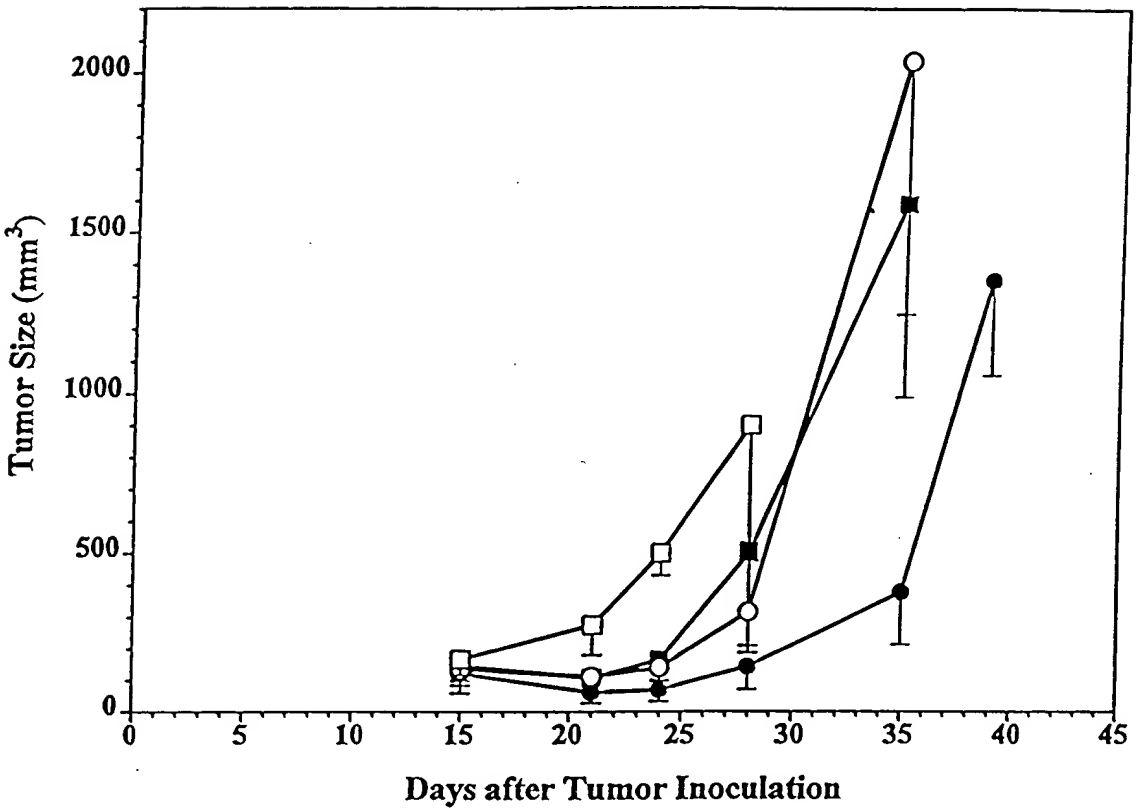

Tumor Size (mm3)
2000
1500
1000
500
0
0
5
10
15
20
25
30
35
40
45
Days after Tumor Inoculation
Control
huN901-DM1
cisplatin + etoposide
huN901 +
cisplatin + etoposide

FIG. 7

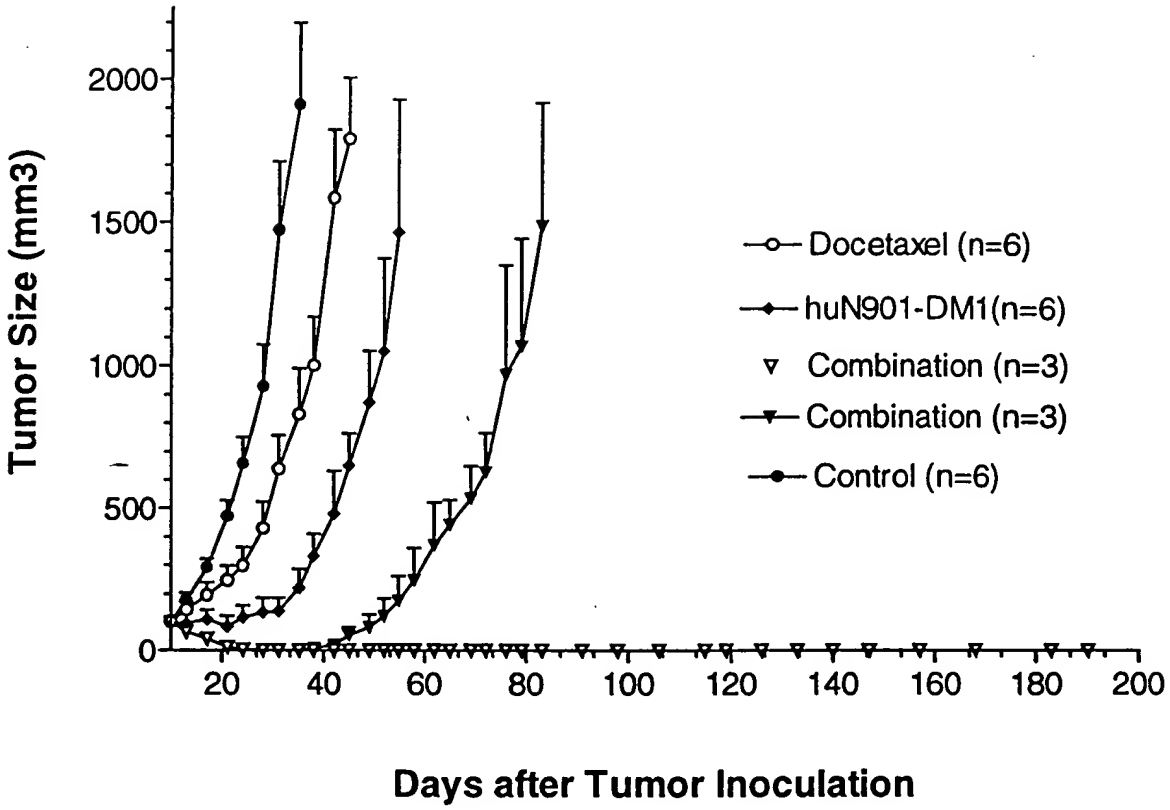

Tumor Size (mm3)
2000
1500
1000
500
0
20
40
60
80
100
120
140
160
180
200
Days after Tumor Inoculation
Docetaxel (n=6)
huN901-DM1(n=6)
Combination (n=3)
Combination (n=3)
Control (n=6)

FIG. 8

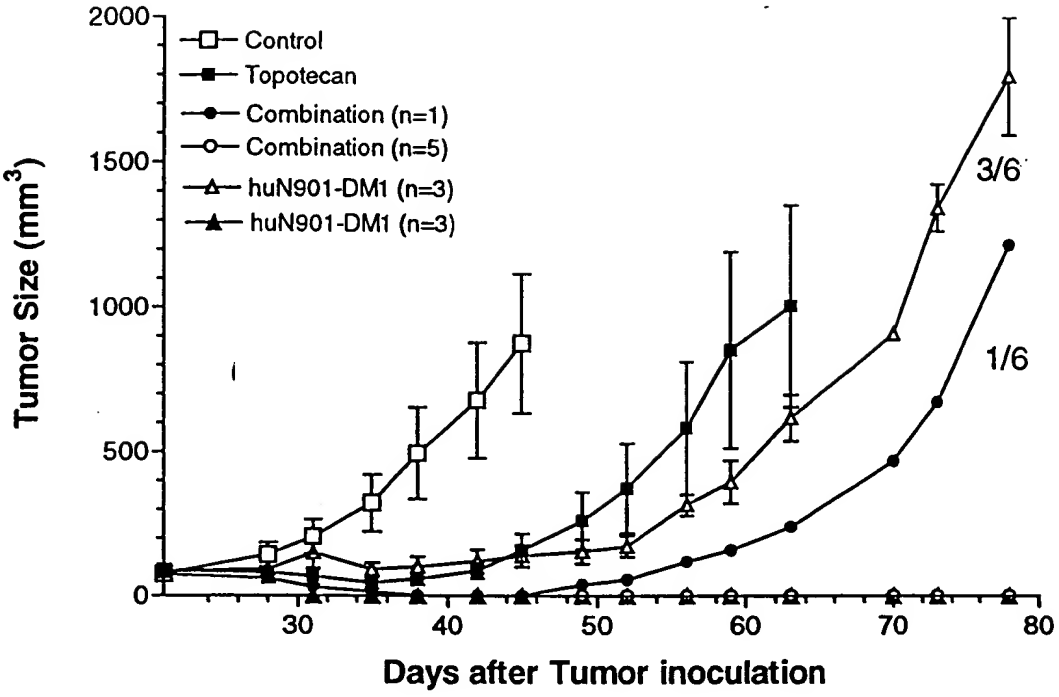

2000
1500
1000
500
0
Tumor Size (mm3)
Control
Topotecan
Combination (n=1)
Combination (n=5)
huN901-DM1 (n=3)
huN901-DM1 (n=3)
3/6
1/6
30
40
50
60
70
80
Days after Tumor inoculation

FIG. 9

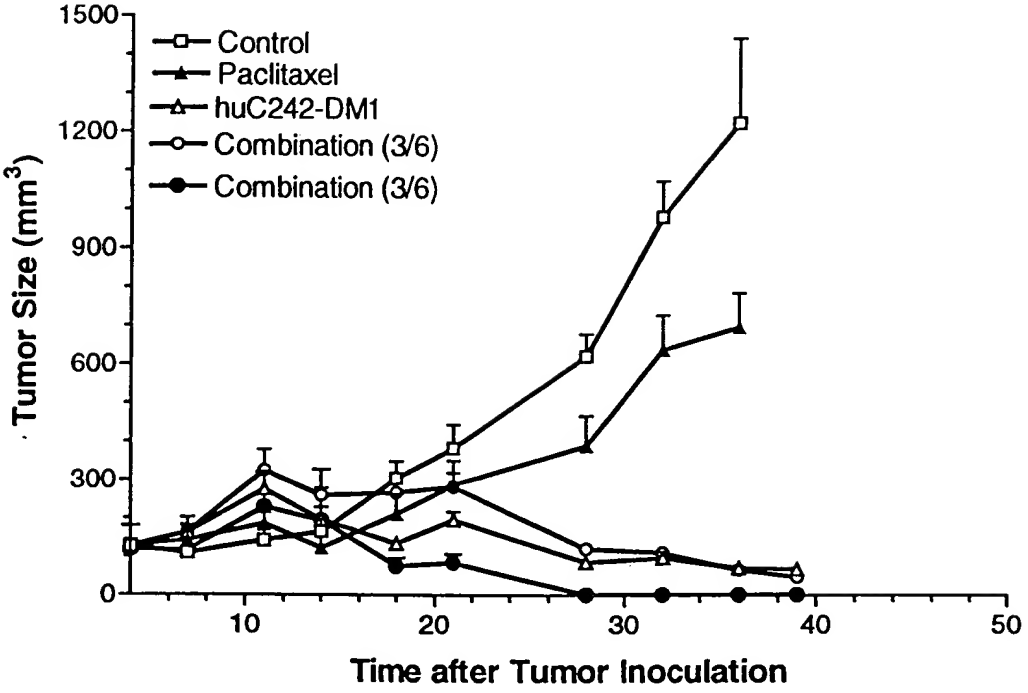
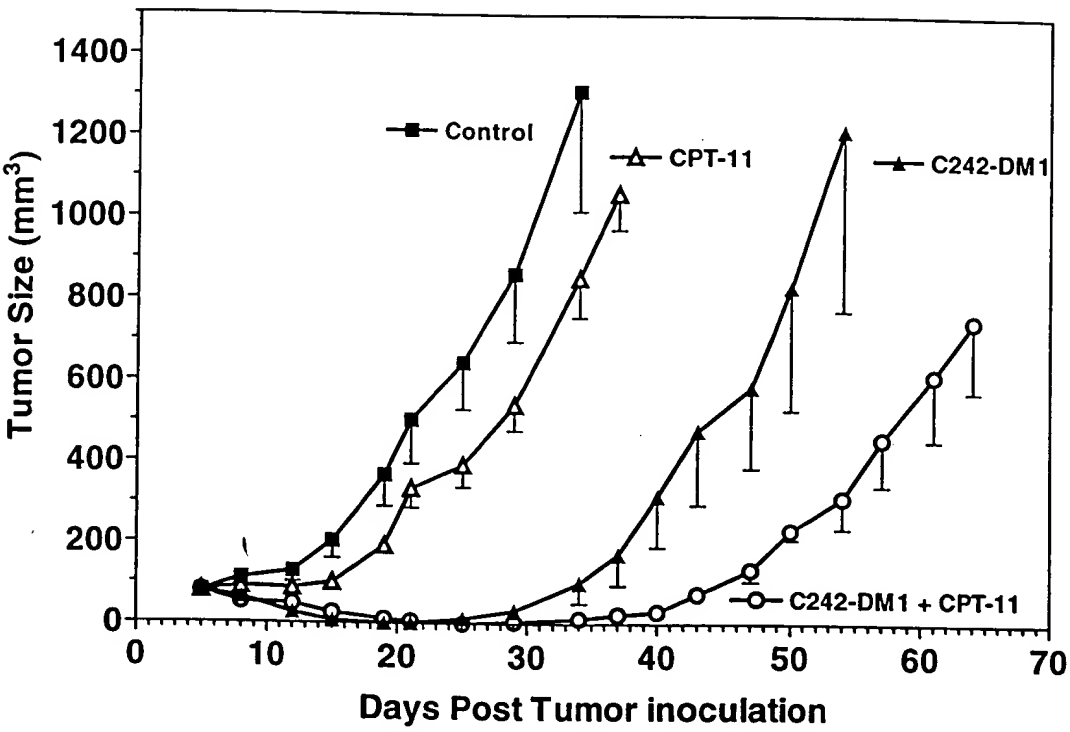

1500
1200
900
600
300
0
Tumor Size (mm3)
Control
Paclitaxel
huC242-DM1
Combination (3/6)
Combination (3/6)
10
20
30
40
50
Time after Tumor Inoculation

FIG. 10


Tumor Size (mm3)
1400
1200
1000
800
600
400
200
0
0
10
20
30
40
50
60
70
Days Post Tumor inoculation
Control
CPT-11
C242-DM1
C242-DM1 + CPT-11